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(54) Title: TREATMENT OF NEOPLASMS WITH VIRUSES

(57) Abstract

The subject invention relates to viruses that are able to replicate and thereby kill neoplastic cells with a deficiency in the IFN-mediated antiviral response, and their use in treating neoplastic disease including cancer and large tumors. RNA and DNA viruses are useful in this regard. The invention also relates to methods for the selection, design, purification and use of such viruses for cancer therapy.

WHAT IS CLAIMED IS:

1. A method of infecting a neoplasm in a mammal with a virus comprising administering an interferon-sensitive, replication-competent clonal RNA virus to said mammal.

2. A method of infecting a neoplasm in a mammal with a virus comprising administering a replication-competent clonal RNA virus to said mammal wherein said virus has sensitivity to interferon.

3. A method of treating a neoplasm in a mammal comprising administering to said mammal a therapeutically effective amount of an interferon-sensitive, replication-competent clonal RNA virus.

4. A method as in claim 1 wherein said RNA virus replicates at least 100-fold less in the presence of interferon compared to in the absence of interferon.

5. A method as in claim 1 wherein said RNA virus replicates at least 1000-fold less in the presence of interferon compared to in the absence of interferon.

6. A method as in claim 1 wherein said administering step is systemic.

7. A method as in claim 1 wherein said neoplasm is a cancer.

8. A method as in claim 1 wherein said mammal is a human.

9. A method as in claim 1 wherein said clonal virus is plaque purified.

10. A method as in claim 1 wherein said clonal virus is of recombinant clonal origin.

11. A method as in claim 1 wherein said RNA virus is a Paramyxovirus.

12. A method as in claim 11 wherein said Paramyxovirus is purified to a level of at least 2×10^9 PFU per mg of protein.

13. A method as in claim 11 wherein said Paramyxovirus is purified to a level of at least 1×10^{10} PFU per mg of protein.

14. A method as in claim 11 wherein said Paramyxovirus is purified to a level of at least 6×10^{10} PFU per mg of protein.

15. A method as in claim 11 wherein said Paramyxovirus is purified to a level in which the particle per PFU ratio is no greater than 5.

16. A method as in claim 11 wherein said Paramyxovirus is purified to a level in which the particle per PFU ratio is no greater than 3.

17. A method as in claim 11 wherein said Paramyxovirus is purified to a level in which the particle per PFU ratio is no greater than 1.2.

18. A method as in claim 11 wherein said Paramyxovirus is avian paramyxovirus type 2.

19. A method as in claim 11 wherein said Paramyxovirus is NDV.

20. A method as in claim 11 wherein said Paramyxovirus is mumps virus.

21. A method as in claim 11 wherein said Paramyxovirus is human parainfluenza virus.

22. A method as claim 1 wherein said RNA virus is selected from the group consisting of a Rhabdovirus, Togavirus, Flavivirus, Reovirus, Picornavirus, and Coronaries.

23. A method as in claim 22 wherein said Togavirus is Sindbis virus.

24. A method as in claim 22 wherein said Reovirus has a modification at omega 3.

25. A method as in claim 22 wherein said Reovirus has an attenuating mutation at omega 1.

26. A method as in claim 22 wherein said Reovirus is an attenuated rotavirus.

27. A method as in claim 26 wherein said rotavirus is rotavirus WC3.

48. A method as in claim 41 wherein said Herpesvirus has a modification in the gamma 34.5 gene and an attenuating mutation in the gene encoding of thymidine kinase, or a deletion in the b'a'c' inverted repeat locus or functionally analogous loci.

49. A method as in claim 41 wherein said Herpesvirus is a Herpesvirus having an attenuating mutation in a gene selected from the group consisting of thymidine kinase, and ribonucleotide reductase, or a deletion in the b'a'c' inverted repeat locus.

50. A method as in claim 1 wherein said neoplasm is a cancer selected from the group consisting of lung, colon, prostate, breast and brain cancer.

51. A method as in claim 1 wherein said neoplasm is a solid tumor.

52. A method as in claim 50 wherein said brain cancer is a glioblastoma.

53. A method as in claim 1 wherein said virus contains a gene encoding interferon to permit the viral expression of interferon.

54. A method as in claim 1 wherein said virus contains a gene encoding a pro-drug activating enzyme.

55. A method as in claim 1 further comprising administering IFN, before, during or after administration of said virus.

56. A method as in claim 55 wherein said interferon is selected from the group consisting of α-IFN, β-IFN, ω-IFN, γ-IFN, and synthetic consensus forms of IFN.

57. A method as in claim 1 further comprising administering a tyrosine kinase inhibitor before, during or after administration of said virus.

58. A method as in claim 1 further comprising administering a compound selected from the group of compounds comprising a purine nucleoside analog, tyrosine kinase inhibitor, cimetidine, and mitochondrial inhibitor.